Drugs Having Double Uses: Medicinals and Pest-Control Agents

(alternative sources for introduction to the environment)

Some chemicals serve double duty as both existing/experimental drugs and as pest-control agents. While this shows the broad utility of certain drugs, it also poses the possibility that these alternative uses serve as additional sources for their introduction to the environment. The potential significance of these alternative uses as sources for environmental release has never been explored. *Examples include:*

- **4-aminopyridine**: experimental multiple sclerosis drug and an **avicide**
- **warfarin**: anticoagulant and a **rat poison**
- **triclosan**: general biocide and **gingivitis agent** used in toothpaste
- **azacholesterols**: antilipidemic drugs and **avian/rodent reproductive inhibitors** [e.g., Ornitrol]
- certain **antibiotics**: used for **orchard pathogens**
- **acetaminophen**: an analgesic and useful for control of **Brown Tree snake**
- **caffeine:** stimulant and approved for control of ***coqui* frog** in Hawaii; also repels and kills snails and slugs at concentrations exceeding 0.5%.

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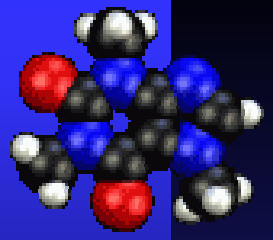


Caffeine for control of frog pests

U.S. EPA approved (27 Sept 2001) specific exemption from FIFRA allowing use of caffeine to control *coqui* frogs in Hawaii.

Exemption allows application of 100-200 pounds per acre (max total 1,200 lbs/year).

In absence of natural predators, *coqui* frog can reproduce to high densities (10,000/acre).

Out-compete native birds by massive consumption of insects.

Chirping frequency is extremely piecing and annoying (upwards of 100 db).

Acetaminophen for control of Brown Tree snakes

Brown Tree snakes (*Boiga irregularis*), native to eastern Indonesia, became invasive pests on Guam starting in the 1940's/1950's.

Without natural predators, the Brown Tree snake's population in Guam is estimated at upwards of 15,000 per square mile.

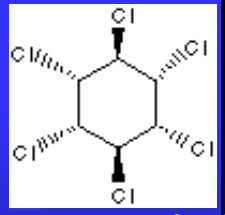
Have decimated certain native bird, bat, and reptile populations, as well as caused extensive economic losses (agriculture, pets, human bites, electric grid outages/repairs).

No safe and effective chemical-controls until discovery by USDA that a**cetaminophen (80 mg) will effectively kill Brown Tree snakes within 3 days** of even a brief exposure to baited, dead mice.

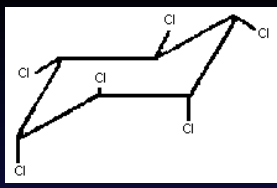
Acute effects of larger doses of acetaminophen on local non-target species have not been detected.

EPA granted registration to USDS-APHIS (March 2003).

[see: J. J. Johnston et al. "Risk Assessment of an Acetaminophen Baiting Program for Chemical Control of Brown Tree Snakes on Guam: Evaluation of Baits, Snake Residues, and Potential Primary and Secondary Hazards," *Environ. Sci. Technol*. 2002, 36(17):3827-3833; also: http://www.aphis.usda.gov/lpa/inside_aphis/features10d.html http://www.aphis.usda.gov/ws/nwrc/is/00pubs/00-66.PDF].



Pesticide Serving as a Therapeutic

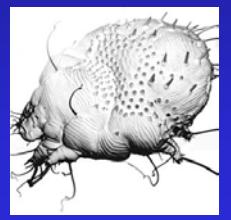


Lindane (*gamma*-HCH, hexachlorocyclohexane) - used since the 1950's for controlling lice (various species of *Pediculus*) and scabies (various mite species of *Sarcoptes*).

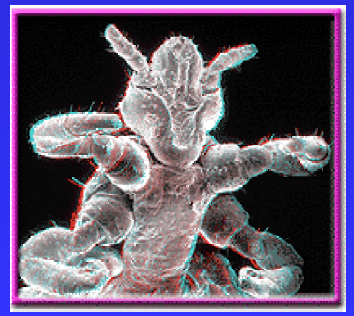
Lindane is one of few organochlorine pesticides still commercially available.

Lindane's topical use (shampoos and lotions) for lice/scabies treatment, especially in children, has extended in recent years also for prophylaxis.

FDA issued public health advisory and mandated a new boxed warning (28 March 2003) for prescription topical lice treatments containing lindane (highlighting neurological risks). To be used with greater caution in children (http://www.fda.gov/cder/drug/infopage/lindane/lindanePHA.htm).



FDA reduced the package size to control imprudent, extended use, and encouraged restricted use as a second-line therapeutic - warranted only when safer alternatives are no longer effective. Patients are sometimes tempted to unsafely extend medication duration because of skin itching (a natural result of the healing process).



EPA Consumer fact sheet on lindane:
http://www.epa.gov/OGWDW/dwh/c-soc/lindane.html

Drugs Having Unintended Ecological Consequences: Secondary Poisoning of Wildlife

- Some drugs, especially those used in veterinary practice, can have unanticipated effects on wildlife, often with drastic consequences.

- A rather well known example is pentobarbital, which is used for animal euthanasia. For extensive information on this topic, see: "Animal Euthanasia and Secondary Wildlife Poisoning" at: http://www.epa.gov/nerlesd1/chemistry/ppcp/greenpharmacy-ref.htm

- But the use of any veterinary drug has the potential for adverse consequences should the animal receiving the medication soon die and its carcass then be fed upon by scavenging wildlife.

- The following slides provide examples.

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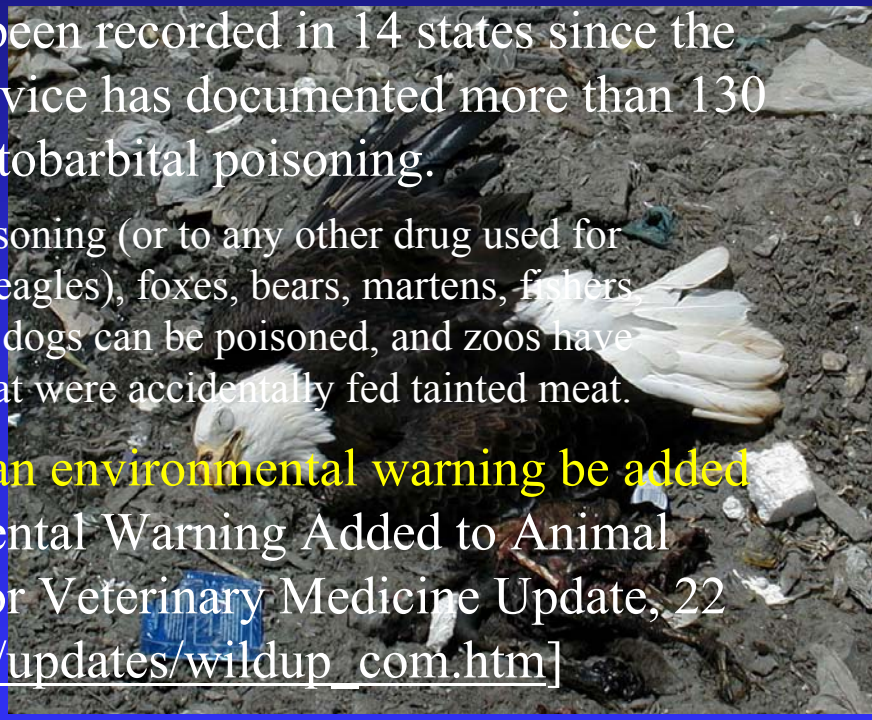
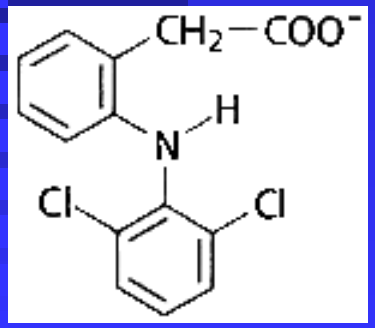
Animal Euthanasia and Secondary Poisoning of Wildlife

- Various drugs are used to euthanize domestic pets and other animals.
- The principle drug is pentobarbital. High doses are used. Most of the body-burden residue escapes excretion and persists indefinitely. The carcass, if not disposed of according to local regulations, can be consumed by scavenger wildlife. But determined wildlife can even uncover well-buried carcasses.
- Wildlife pentobarbital poisonings have been recorded in 14 states since the mid-1980s. The U.S. Fish and Wildlife Service has documented more than 130 bald and golden eagles as casualties of pentobarbital poisoning.
- Wildlife vulnerable to accidental pentobarbital poisoning (or to any other drug used for euthanasia) include a wide range of birds (especially eagles), foxes, bears, martens, fishers, coyotes, lynx, bobcats, cougars, and otters. Domestic dogs can be poisoned, and zoos have documented the deaths of tigers, cougars and lions that were accidentally fed tainted meat.
- In July 2003, the FDA's CVM required an environmental warning be added to animal euthanasia products ["Environmental Warning Added to Animal Euthanasia Products," U.S. FDA, Center for Veterinary Medicine Update, 22 July 2003: htttp://www.fda.gov/cvm/index/updates/wildup_com.htm]
- For background information: see "Animal Euthanasia and Secondary Wildlife Poisoning" at: http://www.epa.gov/nerlesd1/chemistry/ppcp/greenpharmacy-ref.htm



Decline of *Gyps* spp. Vultures in Pakistan & India – Possible Link with Diclofenac

- Beginning in the early 1990s, vultures (especially white-backed vultures such as *Gyps bengalensis*) have experienced dramatic population declines (as great as 95%) in Southern Asia – particularly India and spreading to Pakistan and Nepal.
- Various hypothesized causes have ranged from pathogens to pesticides. The causative agent(s) result in acute renal failure (manifested as visceral gout from accumulation of uric acid), leading to death of the breeding population.
- At the *6th World Conference on Birds of Prey and Owls* (Budapest, Hungary, 18-23 May 2003), Prof. J. Lindsay Oaks (Washington State University) presented evidence that (at least in Pakistan) the die-offs may have resulted from diclofenac poisoning.
- Diclofenac, although primarily a human NSAID, is used in veterinary medicine in certain countries. In India, diclofenac is used for cattle, whose carcasses are a major food source for *Gyps*.



- Diclofenac seems to be selectively toxic to *Gyps* spp. versus other carrion-eating raptors.
- Health hazards grow from the accumulation of uneaten cattle carcasses (as well as human), which now serve to attract growing packs of dangerous feral dogs, which can also carry rabies.